

## **Supplement. Recommendations on Shared Decision Making For Prostate Cancer Screening:**

### **Review of the Literature**

We reviewed published recommendations as to how primary care doctors should implement shared decision-making on prostate cancer screening. We found there to be a pronounced “Goldilocks effect” with recommendations providing either too little information or too much: too little to make an informed decision or so much as to overwhelm patients’ ability to decide rationally.

An example of a recommendation that provides too little information is actually one previously promoted by an author of this recommendation as part of the “ask-tell-ask” rubric (1), that doctors tell patients that “some men will be helped because [an aggressive cancer is cured] but some men will be harmed [by overtreatment]”. As a second example, the American Cancer Society (ACS) has recommended that “core elements of ... information” provided to patients include the statement that “screening may be associated with a reduction in the risk of dying from prostate cancer” and “treatment ... can lead to urinary, bowel, sexual and other health problems [that] may be significant or minimal, permanent or temporary.” (2) The clear problem here is the lack of quantification. There are pros and cons to every course of action; rational decision-making is only possible if the degree of benefit and harm can be compared and balanced.

This has led to attempts to provide quantitative estimates to patients. The National Cancer institute (NCI), for example, has created an infographic based on USPSTF estimates (3), including information such as that, for every 1000 men screened for 10 years, 100 – 120 will have a false positive result (with possible side effects of related biopsy including “serious infections”), 110 will be diagnosed with prostate cancer, of whom 50 will have treatment complications including “erectile dysfunction in 29 men”, “deep vein thrombosis or pulmonary embolism in 1 man” and “death due to treatment in less than 1 man”. On the plus side, “0 – 1 death is avoided.” Other examples of decision aids involving quantitative estimates include those of Giguere et al (4), and Dorfman et al (5).

There are two general problems with such estimates. First, they will be difficult to understand for most patients. For instance, many will fail to understand the implications of a deep vein thrombosis; similarly,

the definition of erectile dysfunction may be unclear (does this mean no erections, or slightly fewer than expected?). It is not apparent that a typical patient could integrate 10 risk estimates for very different events (including erectile dysfunction, “bothersome symptoms from the biopsy”, pulmonary embolism and death) into a sensible decision. Indeed, there is empirical evidence that many patients lack the numerical skills to understand even a single risk estimate, let alone multiple countervailing estimates (6). Furthermore, there are clear data that subtle differences in the way that such numbers are presented can change how patients value different screening outcomes (7).

The second problem with such estimates is that the numbers themselves are highly debatable. For example, there are serious concerns about the NCI’s choice of 10 years as an endpoint, as the effects of PSA screening on mortality increase and effects on overdiagnosis decrease over time (8). One carefully modeled estimate is that 9 lifetime prostate-cancer deaths are avoided per 1000 men choosing to be screened (9) rather than the 0 – 1 given by NCI. Moreover, the estimate of an additional 18 cases of urinary incontinence seems to assume that all men diagnosed with prostate cancer are subject to curative treatment, and that incontinence rates are similar between surgery and radiotherapy. The rates of thromboembolic events and mortality after surgery in the NCI tool are those reported by the USPSTF and are highly questionable, as they are based on cohorts of older men treated 15-20 years ago (10). Of note, quantitative decision aids do not agree with each other, for example, the Giguere et al. decision aid (4) gives 30 extra diagnoses of prostate cancer per 1000 screened compared to 110 from NCI (3).

Problematic statements in recommendations are not restricted to quantitative estimates. One claim made in several guidelines that is particularly inappropriate is that screen-detected prostate cancers cannot be risk stratified. As examples, the ACS states that “it is currently not possible to predict which men are likely to benefit from treatment”; a decision-aid designed for patients states that “there are two types of prostate cancer – harmless and dangerous ... and doctors can’t tell which one a man has ... [moreover] treatment may or may not help men with dangerous prostate cancer” (11). Such claims can only be seen as highly suspect given the long established prognostic value of Gleason grading (12) and the availability

of validated multivariable risk prediction tools (13), as well as clear evidence from randomized trials that mortality reductions associated with treatment are larger for higher risk tumors (14, 15).

Considerable doubts can also be raised about the appropriateness of current recommendations to daily clinical practice. One of the authors of this paper (KE) has conducted extensive interviews with primary care physicians on the topic of PSA screening. A key concern for many was the time it would take to undertake “a detailed discussion of the pros and cons of using the [PSA] test” (NCI recommendations (3)), including uncertainties about key estimates and the importance of different individual values and preferences. For instance, consider the time required to meet a published recommendation that includes 16 separate items of information to impart to the patient (including open ended issues such as discussing “controversies” of screening) and 12 separate questions to ask about preferences (16). Time spent in discussions about PSA is time not spent on other preventive services, resulting in an opportunity cost. Expenditure of considerable amounts of time was also felt to be an inherent bias towards screening: patients felt that doctors would not engage in a long discussion about PSA screening unless they thought that it was worth doing.

Moreover, the value of a “detailed discussion” about PSA depends critically on primary care providers’ knowledge. Less than one in five are confident in their knowledge about PSA, with a low correlation between confidence and actual knowledge (17). Fear of missing a cancer looms large, regardless of how limited the screening capabilities may be. It is perhaps unsurprising then that only about half of primary care physicians are compliant with recommendations to discuss screening with eligible patients (18), with a large proportion adopting a default “screen all” or “screen none” approach.

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## **Evidence Base and Rationale**

***Most men will develop prostate cancer if they live long enough.***

Autopsy studies show that cancer is often found in the prostates of men who die of other causes, > 60% in men over 80. (1)

***Only a small proportion of men with prostate cancer die from the disease.***

The yearly incidence of prostate cancer is about 8 times the yearly mortality rate. (2)

***Screening reduces risk of death from prostate cancer.***

There are two major randomized screening trials. The US-based PLCO trial (3) was described by the authors as a trial of “systematic vs. opportunistic” screening because about half of those in the control group continued to receive PSA tests despite their randomization to a no screening group. The European ERSPC trial had lower rates of contamination, and truly tested the value of screening in men who would not otherwise be screened. In ERSPC, screening led to a 21% relative reduction in the risk of prostate cancer mortality at 11 years. (4) US population trends show that prostate cancer mortality has fallen by over 40% since the introduction of PSA testing (2), an effect difficult to attribute to a cause other than screening (5).

***Screening detects many low risk or "indolent" cancers that do not need treatment.***

In both the ERSPC trial (4) and population-based US data (6) about 60% of cancers were graded as Gleason 6, indicating low risk disease.

***Most low risk cancers do nonetheless end up getting treated.***

About 90% of US patients with low risk prostate cancer are subject to curative treatment. (7)

***Prostate cancer treatment is associated with a risk of serious problems such as incontinence, erectile dysfunction and bowel problems.***

Surgery for prostate cancer can lead to urinary incontinence and erectile dysfunction; radiotherapy is associated with lower rates of erectile dysfunction, but can cause bowel problems. (8)

***Most cancers found by screening don't need to be treated and can be safely managed by careful monitoring***

Most cancers detected by screening are low risk. Longitudinal cohort studies show that patients with low risk prostate cancer managed by active surveillance have extremely low rates of cancer-specific mortality.

(9)

***If you choose to be screened, there is a good chance that you will be diagnosed with a low risk cancer.***

The incidence of prostate cancer in men undergoing screening is approximately 10% at 10 years (4). At least half of these cancers are low risk. (4)

***If you have a low risk cancer, your doctors or your family may pressure you to treat it.***

Most urologists and radiation oncologists, especially those outside academic medical centers, routinely treat almost all low risk cancers (7). Family pressure is commonly reported by clinicians who do promote active surveillance.

***If you are concerned that you would be uncomfortable knowing that you have cancer and not treating it, then screening may not be for you.***

***If you are confident that you would only accept treatment for an aggressive cancer, and would not be unduly worried about a diagnosis of low risk disease, then you are probably a good candidate for screening.***

Most decision-analyses of PSA screening report that the net benefit is borderline (10). Patients who are at high risk of overtreatment are therefore less likely to experience net benefit than those predisposed to choose active surveillance for low risk cancer.

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